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EXAMINER	
KIM, ALEXANDER D	

ART UNIT	PAPER NUMBER
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/812,315	RIEPING, MECHTHILD	
	Examiner	Art Unit	
	ALEXANDER D. KIM	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Sequence Alignment*.

DETAILED ACTION

Prosecution Reopened

1. In view of the Appeal Brief filed on 5/9/2008 and 6/17/2008, PROSECUTION IS HEREBY REOPENED. New grounds of rejection are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below:

/Kathleen Kerr Bragdon/

Supervisory Patent Examiner, Art Unit 1656

Status of the Claims

2. Claims filed on 3/19/2008 were not entered as noted in the Advisory action mailed 5/14/2008. Thus, Claims 13-26 (filed on 9/28/2007, which were entered by the

Advisory action mailed on 10/22/2007) are currently pending and have been considered in this Office Action.

Withdrawn-Claim Objections

3. The previous objection of Claims 13 and 23 for reciting "said bacterium is of the Enterobacteriaceae" (emphasis added) is withdrawn by virtue of Applicant's amendment i.e., reciting "said bacterium is of an Enterobacteriaceae").

4. The previous objection of Claim 15 for reciting the limitation of "comprises the nucleotide sequence of SEQ ID NO: 3" which is identical to the scope of its independent Claim 13 (because Claim 13 also recites the limitation of "comprises the nucleotide sequence of SEQ ID NO: 3") is withdrawn by virtue of Applicants amendment (i.e., reciting "consist of" in Claim 15).

5. The previous objection of Claim 17 for reciting the term "overexpression by increasing the coy number of said DNA" is withdrawn by virtue of the Examiner's reconsideration.

6. The previous objection of Claim 23 for reciting "," (comma) between "starch" and "cellulose" with underline is withdrawn by virtue of Applicant's amendment.

7. The previous objection of Claims 14, 16 and 18-19 because they are dependent from an objected Claim 13 is withdrawn.

Withdrawn-Claim Rejections - 35 USC § 112

8. The previous rejection of Claim 25 under 35 U.S.C. 112, first paragraph, enabling deposit, as failing to comply with the enablement requirement, is withdrawn by virtue of Applicant's argument (i.e., recited bacterial strains are representation of various threonine-producing strains that could be used in connection with the claimed method for producing amino acid).

Claim 25 is enabled by the use of recited biological deposits which were not deposited by the instant Applicants. However, it is noted that the validity of Claim 25 depends on the public availability of said biological deposits. Thus, if at any time said biological deposits become unavailable, Applicants' attention is drawn to the fact that these patent claims may be in question.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 13 (Claims 14-22 dependent therefrom) and 23 (Claims 24-26 dependent therefrom) are rejected under of 35 U.S.C. 112, second paragraph, as being indefinite

for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 13 (Claims 14-22 dependent therefrom) recite limitations "fermenting a bacterium comprising an overexpressed endogenous DNA sequence encoding the galactose-proton symporter protein in said bacterium", "said bacterium is an Enterobacteriaceae family" and "said galactose-proton symporter protein comprises the amino acid sequence of SEQ ID NO: 4 and is encoded by the nucleotide sequence of SEQ ID NO: 3".

Claim 23 (Claims 24-26 dependent therefrom recite limitations "fermenting a bacterium comprising an overexpressed endogenous DNA sequence encoding the galactose-proton symporter protein in said bacterium", "said bacterium is an Enterobacteriaceae family" and "said galactose-proton symporter protein comprises the amino acid sequence of SEQ ID NO: 4".

It is noted that recited bacterium has to be E. coli because the nucleotide SEQ ID NO: 3 and the polypeptide of SEQ ID NO: 4 is the E. coli nucleotide or polypeptide (see instant specification page 10, lines 9-11) when claims require an overexpressed endogenous DNA sequence; wherein there is only one endogenous DNA in the chromosome. It is unclear how any Enterobacteriaceae family other than E. coli can comprises overexpressed endogenous DNA of SEQ ID NO: 3, or a DNA encoding SEQ ID NO: 4.

Appropriate correction is required.

10. Claims 21 and 22 are rejected under of 35 U.S.C. 112, second paragraph, for reciting the limitation “the thrABC operon” or “the tdh gene” (emphasis added) is maintained.

The rejection was stated in the previous office action as it applied to previous Claims 21 and 22. In response to this rejection, applicants have cancelled Claims 1-12; amended Claims 13, 23 and 25; and traverse the rejection as it applies to the newly amended claims.

Applicant argues that the doctrine of equivalents is always used in interpreting the scope of claims even if the claims are confined to a gene from a single species and even if the transitional phrase "consisting of" is used. Applicant also argues that interpreted by courts during litigation and will depend upon a large number of factors and is not usually considered to make claims indefinite (see page 9, Remarks filed on 9/28/2007).

Applicant’s arguments have been fully considered but are not deemed persuasive for the following reasons. The recitation of "the" in front of operon or gene is referring to the one specific operon or gene. As noted in the previous office action, there is insufficient antecedent basis for this limitation in the claim. It is unclear if the claims are limited to the one species disclosed in the specification (see pages 12-15) or to any gene among an equivalents. Claims 21 and 22 would be more appropriate if the claims recite "a thrABC operon” and “a tdh gene", respectively.

Appropriate clarification and/or correction is required.

New-Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter

11. Claim 23 (Claims 24-26 dependent therefrom) is rejected under 35 U.S.C. 112, first paragraph, **new matter**, as failing to comply with the written description requirement. The claim(s) contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 23 recites "transports glucose by a PEP-dependent phosphotransferase (PTS) pathway", which is not supported by the original disclosure. The specification disclose that "PTS enzymes" which may be overexpressed in addition to overexpressing galP gene (see page 12, line 15-20 in the specification), wherein the scope of PTS pathway recited in the claim 32 is different because Claim 32 have said bacterium transports glucose by a PEP-dependent phosphotranferase (PTS) pathway. The applicant is advised to point out the support in the original disclosure or amend the instant claims.

12. Claims 21-22 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 21-22 are drawn to a process of Claim 13, wherein said microorganism overexpresses the thrABC gene or attenuates the tdh gene, respectively.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these (Enzo Biochem 63 USPQ2d 1609 (CAFC 2002)).

University of Rochester v. G.D. Searle & Co. (69 USPQ2d 1886 (2004)) specifically points to the applicability of both Lily and Enzo Biochemical to methods of using products, wherein said products lack adequate written description. While in University of Rochester v. G.D. Searle & Co. the methods were held to lack written description because not a single example of the product used in the claimed methods was described, the same analysis applies wherein the product, used in the claimed methods, must have adequate written description as noted from Enzo Biochemical (see above).

The instant specification discloses a process for the preparation of an L-amino acid by fermenting an *E. coli* transformed with an over-expression vector comprising a nucleic acid encoding the polypeptide of SEQ ID NO: 4; and said method comprising the thrABC operon overexpression by over-expression vector thereby increasing the gene copy number or a method comprising an E. coli that reduce the tdh gene expression by homologous recombination thereby deleting said tdh gene from the chromosome. However, the breadth of Claim 21 includes a method comprising using an Enterobacteriaceae family having increased catalytic activity of enzymes from the thrABC operon according to the disclosure of the term "overexpression" on p. 7, line 1-5. The breadth of Claim 22 encompasses a method comprising using any Enterobacteriaceae family by reducing or switching off of intracellular activity; wherein the activity encompasses the transporting activity of the enzyme encoded by the tdh gene suggested by the specification on page 16, line 23. As noted above, the instant specification discloses a process for the production of an L-amino acids by

overexpressing the galactose-proton symporter protein of SEQ ID NO: 4 by transforming the vector which expresses the SEQ ID NO: 4 into an E. coli; wherein the process of making L-amino acid comprising an E. coli that overexpresses the thrABC operon using overexpression vector thereby increasing the gene copy number; or the E. coli that attenuates the tdh gene by homologous recombination thereby deleting out said tdh gene from the chromosome. However, the instant specification and prior art failed to teach a representative species of claimed method in Claims 21-22 which encompass very broad genus process comprising bacteria having the enzyme(s) encoded by thrABC operon with increased catalytic activity; or reduced catalytic activity of the enzyme encoded by the tdh gene. Also, the deletion of said tdh gene from the chromosome by homologous recombination from a chromosome requires the sequence information of said tdh nucleotides in any Enterobacteriaceae, wherein the instant specification or the prior art does not teach adequate species the tdh gene sequence from any Enterobacteriaceae. The instant specification also does not disclose a single example of using bacteria having the tdh gene with reduced catalytic activity. Thus, there is no correlation between the structure of said genes and the function of increasing, or reducing the catalytic activity of the protein encoded by the genes in Claims 21-22. Thus, one skilled in the art would not be in possession of the full scope of claimed genus method by the instant specification.

13. Claims 21-22 are rejected under 35 U.S.C. 112, first paragraph, scope of enablement, because the specification, while being enabling for a process for the

producing L-amino acid using an *Enterobacteriaceae* family comprising overexpression of SEQ ID NO: 4 and overexpression of the thrABC operon wherein the overexpression is achieved by an overexpression vector and transforming into *Enterobacteriaceae* family; or a process for the producing L-amino acid using an *E. coli* comprising attenuation of the tdh gene wherein the attenuation is achieved by a homologous recombination thereby knocking out said tdh gene; does **not** reasonably provide enablement for a process for the producing L-amino acid comprising: an *Enterobacteriaceae* family having increased catalytic activity of enzymes encoded by the thrABC operon, or a process for the producing L-amino acid using any *Enterobacteriaceae* family having decreased catalytic activity of enzyme encoded by the tdh gene.

The specification does not enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and use of the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single,

simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The nature of the invention is drawn to a process for the production of an L-amino acid using an *Enterobacteriaceae* family with overexpression of the galactose-proton symporter protein of SEQ ID NO: 4 and additionally having overexpression of the thrABC gene wherein the overexpression is achieved by an overexpression vector and transforming into *Enterobacteriaceae* family, or additionally attenuating the tdh gene wherein the attenuation is achieved by a homologous recombination thereby knocking out said tdh gene in E. coli. However, the breadth of Claim 21 encompasses very broad genus process comprising using an Enterobacteriaceae family having increased catalytic activity of enzymes from the thrABC operon according to the disclosure of the term "overexpression" on p. 7, line 1-5. The breadth of Claim 22 encompasses a method comprising using any Enterobacteriaceae family by reducing or switching off of intracellular activity; wherein the activity encompasses the transporting activity of the enzyme encoded by the tdh gene suggested by the specification on page 16, line 23. The instant specification and prior art disclose no direction or guidance on how to make

any protein with increased catalytic activity or decreased catalytic activity. Also, the deletion of said tdh gene from the chromosome by homologous recombination from a chromosome requires the sequence information of said tdh nucleotides in any Enterobacteriaceae family, wherein the instant specification or the prior art does not teach the tdh gene sequence of any Enterobacteriaceae family. Thus, the specification discloses neither a single working example of a protein with increased catalytic activity or decreased catalytic activity. Because complex nature of enzyme catalysis and number of amino acids involved in catalysis, it is unpredictable for one skilled in the art to increase catalytic activity or decrease catalytic activity of any enzyme is highly unpredictable. The said unpredictability makes the relative skill required in the art very high. For all of the above reason, it would require undue experimentation necessary to make and use the full scope of claimed methods.

Withdrawn-Claim Rejections - 35 USC § 102

14. The previous rejection of Claims 23-24 and 26 under 35 U.S.C. 102(b) as being anticipated by Valle et al. (USPAP 2002/0155521 published on Oct. 24, 2002, as cited in the previous Office Action) as evidenced by Blattner et al. (1997, Science 277:1453-1474, as cited in the IDS) is withdrawn by virtue of Applicant's argument (i.e., there is only one glucose transport pathway in cells that is termed the PEP-dependent phosphotransferase (PTS) pathway and this pathway does not includes the galactose-proton symporter protein, see middle of page 11, Remarks filed on 9/28/2007); the cell used by Valle et al. is an E. coli with PTS^- strain.

15. The previous rejection Claims 23-24 and 26 under 35 U.S.C. 102(a) as being anticipated by Hernandez-Montalvo et al. (2003 Sep. 20, Biotechnol Bioeng, Vol. 83, page 687-694) as evidenced by Blattner et al. (1997, Science 277:1453-1474, as cited in the IDS) and Lee et al. (2003, September, Journal of Bacteriology, vol. 185, p. 5442-5451) is withdrawn by virtue of Applicant's argument (i.e., there is only one glucose transport pathway in cells that is termed the PEP-dependent phosphotransferase (PTS) pathway and this pathway does not includes the galactose-proton symporter protein, see middle of page 11, Remarks filed on 9/28/2007); the cell used by Hernandez-Montalvo et al. is an E. coli with PTS^- strain.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claim 13-16, 18-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Valle et al. (USPAP 2002/0155521 published on Oct. 24, 2002, as cited in the previous Office Action) as evidenced by Blattner et al. (1997, Science 277:1453-1474, as cited in the IDS).

Claims 13 (Claims 14-22 dependent therefrom) are drawn to a process for the production of an L-amino acid comprising:

a) fermenting a bacterium comprising an overexpressed endogenous DNA sequence encoding the galactose-proton symporter protein in said bacterium, in a fermentation medium under conditions suitable for the production of said L- amino acid, wherein: i) said bacterium is of an Enterobacteriaceae family; ii) said galactose-proton symporter protein comprises the amino acid sequence of SEQ ID NO:4 and is encoded by the nucleotide sequence of SEQ ID NO:3; iii) said L-amino acid is produced from glucose, saccharose, lactose, fructose, molasses, starch, cellulose or from glycerine and ethanol; iv) said overexpression is achieved by increasing the copy number of said DNA or by operably linking said DNA to a promoter; and

b) allowing said L-amino acid to become enriched in said bacteria or said fermentation medium.

The recitation of "the nucleotide sequence of SEQ ID NO: 3" can be interpreted as referring to an entire nucleotide sequence of SEQ ID NO: 3 in Claim 13. The recitation of "an overexpressed endogenous DNA sequence encoding" encompasses any overexpressed DNA sequence and said DNA sequence is not limited to the nucleotide of SEQ ID NO: 3 because the recitation of "the nucleotide sequence of SEQ ID NO: 3" can be interpreted as only describing the amino acid sequence of SEQ ID NO: 4 and not necessarily referring to the endogenous DNA sequence. Thus, the claimed process does not require the bacterium must present the nucleotide sequence

of SEQ ID NO: 3 (i.e., the entire nucleotide sequence of SEQ ID NO: 3); wherein the SEQ ID NO: 3 is recited in Claims 13, 15 and 16.

Claims 13, 15 and 16; and said claims are unclear because the nucleotide sequence of SEQ ID NO: 3 (i.e., the entire nucleotide sequence of SEQ ID NO: 3) does not encodes the amino acid of SEQ ID NO: 4. For the examination purpose, "encoded by the nucleotide sequence of SEQ ID NO: 3" (Claim 13) or "consist of the nucleotide sequence of SEQ ID NO; 3" (Claims 15-16) is interpreted as the coding sequence of SEQ ID NO: 3 (i.e., 33-1427 residues in SEQ ID NO: 3) is encoding the polypeptide of SEQ ID NO: 4, if necessary.

Valle et al. teach that "the Pts^-/$glucose^+$ strain, glucose transport occurs via the galactose permease, encoded by galP. The galR and galS genes encode the repressor and is repressor, respectively, of the gal operon [31], and galR is known to repress expression of the galP gene [25]. Thus, inactivation of the galR (and possibly the galS) gene in the Pts^- background should lead to de-repression of the galactose permease and a $glucose^+$ phenotype" (see Example 5, on page 8, middle of right column). Valle et al. teach the PB115 (i.e., derepressed galR and galS to express galP) which results in pink colonies on MacConkey-agar containing 1% glucose; wherein the pink color indicates "that the ability to transport glucose and secrete organic acids had been partially restored" (see page 8, middle of right column); wherein the ability to use the glucose is results of galP gene overexpression compared to the PB114 having white colony which is the indication of lacking expression of galP results in not being able to transport and utilize the glucose according to the Table 5 on page 8. The colony

formation on the MacConkey-agar containing 1% glucose by the E. coli PB115 meets the limitation of steps: fermenting a bacterium and inherently allowing said L-amino acids (including the L-threonine as shown by graphs in Figure 1 which disclose the threonine biosynthetic pathway starting from glucose) to become enriched in said bacteria. The sequence of overexpressed E. coli GalP protein of Valle et al. is 100% identical to the SEQ ID NO: 4 (and to the encoding region of SEQ ID NO: 3) as evidenced by Blattner et al. (see the Sequence Alignment in the attachment). The fact that E. coli PB115 expresses the galP to transport glucose and utilize (as evidenced by pink color) teach that the galP gene is operably linked to a promoter. Thus, the method of growing E. coli PB115 by Valle et al. meets the limitation of Claims 13-16, 18. The growth of each isolated pink colony by E. coli PB115 on the agar is also encompassed by the Claims 19-20 because said claims encompasses a process of any claims 13-16, further comprising isolating said L-amino acid along with all of the constituents of said fermentation medium and/or the biomass in said fermentation medium (emphasis added).

17. Claims 13-14 and 17-20 are rejected under 35 U.S.C. 102(a) as being anticipated by Hernandez-Montalvo et al. (2003 Sep. 20, Biotechnol Bioeng, Vol. 83, page 687-694, as cited previously on 12/13/2006) as evidenced by Blattner et al. (1997, Science 277:1453-1474, as cited in the IDS) and Lee et al. (2003, September, Journal of Bacteriology, vol. 185, p. 5442-5451, as cited previously on 12/13/2006).

Applicants have provided the certified translation of Germany application 103 14 618.0 on 3/14/2008 to overcome previous rejection by Hernandez-Montalvo et al (see the Office Action mailed on 12/13/2006). Said Germany application does not disclose the SEQ ID NO: 3 and SEQ ID NO: 4 and disclose the sequence of E. coli galP gene can be obtained from the reference of Blattner et al. (1997) which only describes the naturally occurring gene. However, as written in Claim 13, the full length of SEQ ID NO: 3 contain the N-terminal sequence (1-13) which is not a naturally occurring DNA sequence in the E. coli (see Sequence Alignment against Blattner et al. in the attachment). Thus, Germany application 103 14 618.0 does not have support for the full length nucleotide sequence of SEQ ID NO: 3. Instant filing date of 03/30/2004 is the priority date for the instant Claim 13 (Claims 14-22 dependent therefrom.

Claims 13 (Claims 14 and 17-20 dependent therefrom) are drawn to a process for the production of an L-amino acid comprising:

a) fermenting a bacterium comprising an overexpressed endogenous DNA sequence encoding the galactose-proton symporter protein in said bacterium, in a fermentation medium under conditions suitable for the production of said L- amino acid, wherein: i) said bacterium is of an Enterobacteriaceae family; ii) said galactose-proton symporter protein comprises the amino acid sequence of SEQ ID NO:4 and is encoded by the nucleotide sequence of SEQ ID NO:3; iii) said L-amino acid is produced from glucose, saccharose, lactose, fructose, molasses, starch, cellulose or from glycerine

and ethanol; iv) said overexpression is achieved by increasing the copy number of said DNA or by operably linking said DNA to a promoter; and

b) allowing said L-amino acid to become enriched in said bacteria or said fermentation medium.

Claims 13-14 and 18-20 are process of Claim 13 with additional limitation as recited in claims.

Hernandez-Montalvo et al. teach a method of making a plasmid “containing E. coli galP” and used to transform E. coli (see left column middle, page 687). The transformed E. coli (see Table 1), which is a derivative of strain W3110 (p. 689, left column, bottom), “was used to evaluate the roles of GalP” (see right column, bottom, page 688. The “Cells were grown in Luria-Bertani (LB) broth or LB agar plates” which comprises a glucose, “for all the recombinant DNA techniques” (see right column bottom on page 688 to left column top on page 689) or in M9 minimal media comprising 0.2 glucose (see middle of left column, p. 690). Hernandez-Montalvo et al. teach “the effect of increased GalP” “on growth capacity with glucose for a PTS^- strain, the transformed strains, with plasmids carrying the trc promoter set controlling galP and glk expression” wherein the galP gene is overexpressed (page 691, right column, top) (see right column bottom, page 690). Thus, Hernandez-Montalvo et al. teach a process of inherent production of L-Thr as evidenced by Lee et al. who disclose E. coli strain W3110 produces L-threonine as shown in Table 5, page 5450. Although, the recitation of "the nucleotide sequence of SEQ ID NO: 3" can be interpreted as only describing the

amino acid sequence of SEQ ID NO: 4 and not necessarily referring to the endogenous DNA sequence; and because the SEQ ID NO: 3 contains extra nucleotides which is not translated into the encoded polypeptide of SEQ ID NO: 3; Claim 13 has been interpreted as the coding sequence of SEQ ID NO: 3 (i.e., 33-1427 residues in SEQ ID NO: 3) is encoding the polypeptide of SEQ ID NO: 4, if necessary. The E. coli GalP protein is identical to SEQ ID NO: 4 and is encoded by the coding sequence in SEQ ID NO: 3 as evidenced by Blattner et al. as shown in Sequence Alignment (see attachment). The growth of the transformed cell of Hernandez-Montalvo et al. meets the limitation of fermenting and allowing said L-amino acid to become enriched in said bacteria in Claims 13-18 and 20. Hernandez-Montalvo et al. also teach a method step of "high-performance liquid chromatography" from a cell culture (see top right column, page 690), which inherently meets limitation of isolating said L-amino acid along with some or all of the constituents of said fermentation medium and/or the biomass in Claim 19.

Claim Rejections - 35 USC § 103

18. Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Valle et al. (USPAP 2002/0155521 published on Oct. 24, 2002, as cited in the previous Office Action) in view of Debabov et al. (USP 6,132,999 published on Oct. 17, 2000, as cited in the previous Office Action).

Valle et al. disclose the teachings as described above. Valle et al. also teach L-amino acids including L-threonine production form glucose could be enhanced in the Pts^-/$glucose^+$ E. coli strain according to the biosynthetic pathway in Figure 1.

Valle et al. does not teach overexpression of the thrABC operon in the E. coli strain for L-Thr production.

Debabov et al. (2000) teach a process of improved amino acid production by transforming an E. coli with an expression vector comprising a threonine operon (thrABC), which overexpresses the thrABC gene product. Debavov et al. (2000) teach a process of making L-threonine by using E. coli BKIIM B-5318 in Example 1. The E. coli BKIIM B-5318 has "plasmid pPRT614, which has threonine biosynthesis genes (thrA, B, and C)" as disclosed in the Abstract.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to increase expression of galP encoding galactose permease of Valle et al. and additionally overexpress thrABC operon of Debabov et al. by transforming the PTS-/$glucose^+$ E. coli of Valle with the expression vector encoding thrABC of Debabov et al. The motivation to do so is provided by Valle et al. who teaches the usefulness of cost-effective and efficient biosynthetic production of compounds or derivative" (see column 0003, lines 1-2) using the Pts^-/$glucose^+$ GalP strain of Valle et al. for producing L-Thr (paragraph 5, bottom) and that overexpession of thrABC operon results in enhanced L-Thr production as taught by Debabov. One would have had a reasonable expectation of success for overexpressing thrABC operon in the Pts^-/$glucose^+$ strain of Valle et al. because of the teachings of Debabov et al. and Valle

et al. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

19. Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Valle et al. (USPAP 2002/0155521 published on Oct. 24, 2002) in view of Debavov et al. (USP 5,705371 published on Jan. 6, 1998).

Valle et al. disclose the teachings as described above. Valle et al. also teach L-amino acids including L-threonine production form glucose could be enhanced in the Pts^-/$glucose^+$ E. coli strain according to the biosynthetic pathway in Figure 1.

Valle et al. does not teach attenuation of the tdh gene.

Debavov et al. (1998) teach a process of making L-threonine by attenuation of the tdh gene encoding a threonine dehydrogenase "engaged in degradation of L-threonine" (see column 2, lines 58-59). Debavov et al. (1998) teach "E. coli strain VNIIgenetika 472T23" having "insertion of transposon Tn5 into gene tdh " is "devoid completely of activity" of a threonine dehydrogenase (see column 2, line 53-59).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to attenuate the tdh gene of Debavov et al. (1998) in the Pts^-/$glucose^+$ strain of Valle et al. The motivation to do so is provided by Valle et al. and Debabov et al. (1998) who teach the usefulness of "the cost-effective and efficient biosynthetic production of compounds or derivative" (see §0003 lines 1-2) by increasing the production of L-amino acid in E. coli, that L-Thr production could be enhanced in a Pts^-/$glucose^+$ strain, and that attenuation of tdh attenuates production of a

polypeptide that degrades L-Thr. One would have had a reasonable expectation of success for attenuating a tdh gene in the Pts^-/$glucose^+$ strain of Valle et al. because of the teachings of Debabov et al. and Valle et al. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Conclusion

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALEXANDER D. KIM whose telephone number is (571)272-5266. The examiner can normally be reached on 11AM-7:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on (571) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Alexander D Kim/
Examiner, Art Unit 1656

/Kathleen Kerr Bragdon/
Supervisory Patent Examiner, Art Unit 1656

Sequence Alignment

```
10/812315
RESULT 2
GALP_ECOLI
ID   GALP_ECOLI     STANDARD;      PRT;   464 AA.
AC   P0AEP1; P37021;
DT   20-DEC-2005, integrated into UniProtKB/Swiss-Prot.
DT   20-DEC-2005, sequence version 1.
DT   07-MAR-2006, entry version 5.
DE   Galactose-proton symporter (Galactose transporter).
GN   Name=galP; OrderedLocusNames=b2943;
OS   Escherichia coli.
OC   Bacteria; Proteobacteria; Gammaproteobacteria; Enterobacteriales;
OC   Enterobacteriaceae; Escherichia.
OX   NCBI_TaxID=562;
RN   [1]
RP   NUCLEOTIDE SEQUENCE [GENOMIC DNA], AND CHARACTERIZATION.
RA   Roberts P.E.;
RL   Thesis (1992), University of Cambridge, United Kingdom.
RN   [2]
RP   NUCLEOTIDE SEQUENCE [LARGE SCALE GENOMIC DNA].
RC   STRAIN=K12 / MG1655;
RX   MEDLINE=97426617; PubMed=9278503; DOI=10.1126/science.277.5331.1453;
RA   Blattner F.R., Plunkett G. III, Bloch C.A., Perna N.T., Burland V.,
RA   Riley M., Collado-Vides J., Glasner J.D., Rode C.K., Mayhew G.F.,
RA   Gregor J., Davis N.W., Kirkpatrick H.A., Goeden M.A., Rose D.J.,
RA   Mau B., Shao Y.;
RT   "The complete genome sequence of Escherichia coli K-12.";
RL   Science 277:1453-1474(1997).
RN   [3]
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RC   STRAIN=K12 / MG1655;
RX   PubMed=15919996; DOI=10.1126/science.1109730;
RA   Daley D.O., Rapp M., Granseth E., Melen K., Drew D., von Heijne G.;
RT   "Global topology analysis of the Escherichia coli inner membrane
RT   proteome.";
RL   Science 308:1321-1323(2005).
CC   -!- FUNCTION: Uptake of galactose across the boundary membrane with
CC       the concomitant transport of protons into the cell (symport
CC       system).
CC   -!- SUBCELLULAR LOCATION: Bacterial cell inner membrane; multi-pass
CC       membrane protein.
CC   -!- SIMILARITY: Belongs to the major facilitator superfamily. Sugar
CC       transporter family.
CC   ----------------------------------------------------------------------
CC   Copyrighted by the UniProt Consortium, see http://www.uniprot.org/terms
CC   Distributed under the Creative Commons Attribution-NoDerivs License
CC   ----------------------------------------------------------------------
DR   EMBL; U28377; AAA69110.1; -; Genomic_DNA.
DR   EMBL; U00096; AAC75980.1; -; Genomic_DNA.
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DR   GenomeReviews; U00096_GR; b2943.
DR   EchoBASE; EB2068; -.
DR   EcoGene; EG12148; galP.
DR   BioCyc; EcoCyc:GALP-MONOMER; -.
DR   LinkHub; P37021; -.
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DR   PROSITE; PS00216; SUGAR_TRANSPORT_1; 1.
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KW   Transmembrane; Transport.
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FT                                /FTId=PRO_0000050292.
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FT   TRANSMEM     16     36       1 (Potential).
FT   TOPO_DOM     37     56       Periplasmic (Potential).
FT   TRANSMEM     57     77       2 (Potential).
FT   TOPO_DOM     78     84       Cytoplasmic (Potential).
FT   TRANSMEM     85    105       3 (Potential).
FT   TOPO_DOM    106    112       Periplasmic (Potential).
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FT   TOPO_DOM    134    139       Cytoplasmic (Potential).
FT   TRANSMEM    140    160       5 (Potential).
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FT   TOPO_DOM    193    250       Cytoplasmic (Potential).
FT   TRANSMEM    251    271       7 (Potential).
FT   TOPO_DOM    272    290       Periplasmic (Potential).
FT   TRANSMEM    291    311       8 (Potential).
FT   TOPO_DOM    312    321       Cytoplasmic (Potential).
FT   TRANSMEM    322    342       9 (Potential).
FT   TOPO_DOM    343    351       Periplasmic (Potential).
FT   TRANSMEM    352    372       10 (Potential).
FT   TOPO_DOM    373    394       Cytoplasmic (Potential).
FT   TRANSMEM    395    415       11 (Potential).
FT   TOPO_DOM    416    416       Periplasmic (Potential).
FT   TRANSMEM    417    437       12 (Potential).
FT   TOPO_DOM    438    464       Cytoplasmic (Potential).
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VERSION     U00096.2  GI:48994873
KEYWORDS    .
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  ORGANISM  Escherichia coli K12
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REFERENCE   1  (bases 1 to 4639675)
  AUTHORS   Blattner,F.R., Plunkett,G., Bloch,C.A., Perna,N.T., Burland,V.,
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            Gregor,J., Davis,N.W., Kirkpatrick,H.A., Goeden,M.A., Rose,D.J.,
            Mau,B. and Shao,Y.
  TITLE     The complete genome sequence of Escherichia coli K-12
  JOURNAL   Science 277 (5331), 1453-1474 (1997)
   PUBMED   9278503
REFERENCE   2  (bases 1 to 4639675)
  AUTHORS   Riley,M., Abe,T., Arnaud,M.B., Berlyn,M.K., Blattner,F.R.,
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            Mori,H., Perna,N.T., Plunkett,G. III, Rudd,K.E., Serres,M.H.,
            Thomas,G.H., Thomson,N.R., Wishart,D. and Wanner,B.L.
  TITLE     Escherichia coli K-12: a cooperatively developed annotation
            snapshot--2005
  JOURNAL   (er) Nucleic Acids Res. 34 (1), 1-9 (2006)
   PUBMED   16397293
REFERENCE   3  (bases 1 to 4639675)
  AUTHORS   Arnaud,M., Berlyn,M.K.B., Blattner,F.R., Galperin,M.Y.,
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            Wanner,B.L.
  TITLE     Workshop on Annotation of Escherichia coli K-12
  JOURNAL   Unpublished
  REMARK    Woods Hole, Mass., on 14-18 November 2003 (sequence corrections)
REFERENCE   4  (bases 1 to 4639675)
  AUTHORS   Glasner,J.D., Perna,N.T., Plunkett,G. III, Anderson,B.D.,
            Bockhorst,J., Hu,J.C., Riley,M., Rudd,K.E. and Serres,M.H.
  TITLE     ASAP: Escherichia coli K-12 strain MG1655 version m56
  JOURNAL   Unpublished
  REMARK    ASAP download 10 June 2004 (annotation updates)
REFERENCE   5  (bases 1 to 4639675)
  AUTHORS   Hayashi,K., Morooka,N., Mori,H. and Horiuchi,T.
  TITLE     A more accurate sequence comparison between genomes of Escherichia
            coli K12 W3110 and MG1655 strains
  JOURNAL   Unpublished
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  REMARK    GenBank accessions AG613214 to AG613378 (sequence corrections)
REFERENCE   6  (bases 1 to 4639675)
  AUTHORS   Perna,N.T.
  TITLE     Escherichia coli K-12 MG1655 yqiK-rfaE intergenic region, genomic
            sequence correction
  JOURNAL   Unpublished
  REMARK    GenBank accession AY605712 (sequence corrections)
REFERENCE   7  (bases 1 to 4639675)
  AUTHORS   Rudd,K.E.
  TITLE     A manual approach to accurate translation start site annotation: an
            E. coli K-12 case study
  JOURNAL   Unpublished
REFERENCE   8  (bases 1 to 4639675)
  AUTHORS   Blattner,F.R. and Plunkett,G. III.
  TITLE     Direct Submission
  JOURNAL   Submitted (16-JAN-1997) Laboratory of Genetics, University of
            Wisconsin, 425G Henry Mall, Madison, WI 53706-1580, USA
REFERENCE   9  (bases 1 to 4639675)
  AUTHORS   Blattner,F.R. and Plunkett,G. III.
  TITLE     Direct Submission
  JOURNAL   Submitted (02-SEP-1997) Laboratory of Genetics, University of
            Wisconsin, 425G Henry Mall, Madison, WI 53706-1580, USA
REFERENCE   10 (bases 1 to 4639675)
  AUTHORS   Plunkett,G. III.
  TITLE     Direct Submission
  JOURNAL   Submitted (13-OCT-1998) Laboratory of Genetics, University of
            Wisconsin, 425G Henry Mall, Madison, WI 53706-1580, USA
REFERENCE   11 (bases 1 to 4639675)
  AUTHORS   Plunkett,G. III.
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            Wisconsin, 425G Henry Mall, Madison, WI 53706-1580, USA
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                     /sub_strain="MG1655"
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ORIGIN
//
Disclaimer | Write to the Help Desk
NCBI | NLM | NIH
```

Sequences producing significant alignments:	Score (Bits)	E Value
gi|85674274|dbj|AP009048.1| Escherichia coli W3110 DNA, complete	2841	0.0
gi|48994873|gb|U00096.2| Escherichia coli K12 MG1655, complete g	2841	0.0
gi|882431|gb|U28377.1|ECU28377 Escherichia coli K-12 genome; app	2841	0.0
gi|81244029|gb|CP000036.1| Shigella boydii Sb227, complete genom	2785	0.0
gi|73854091|gb|CP000038.1| Shigella sonnei Ss046, complete genom	2769	0.0
gi|81239530|gb|CP000034.1| Shigella dysenteriae Sd197, complete	2714	0.0
gi|110341805|gb|CP000247.1| Escherichia coli 536, complete genom	2698	0.0
gi|26111730|gb|AE014075.1| Escherichia coli CFT073, complete gen	2690	0.0
gi|115511419|gb|CP000468.1| Escherichia coli APEC O1, complete g	2674	0.0
gi|110613622|gb|CP000266.1| Shigella flexneri 5 str. 8401, compl	2674	0.0
gi|91070629|gb|CP000243.1| Escherichia coli UTI89, complete geno	2674	0.0
gi|24080789|gb|AE005674.1| Shigella flexneri 2a str. 301, comple	2674	0.0
gi|30043918|gb|AE014073.1| Shigella flexneri 2a str. 2457T, comp	2674	0.0
gi|47118301|dbj|BA000007.2| Escherichia coli O157:H7 str. Sakai	2635	0.0
gi|56384585|gb|AE005174.2| Escherichia coli O157:H7 EDL933, comp	2635	0.0
gi|16421636|gb|AE008842.1| Salmonella typhimurium LT2, sectio...	1211	0.0
gi|16504049|emb|AL627277.1| Salmonella enterica serovar Typhi...	1195	0.0
gi|29140506|gb|AE014613.1| Salmonella enterica subsp. enteric...	1195	0.0
gi|62126203|gb|AE017220.1| Salmonella enterica subsp. enteric...	1187	0.0
gi|56126533|gb|CP000026.1| Salmonella enterica subsp. enteric...	1179	0.0

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>gi|85674274|dbj|AP009048.1|  Escherichia coli W3110 DNA, complete genome
Length=4646332

 Features in this part of subject sequence:
   D-galactose transporter

 Score = 2841 bits (1433),  Expect = 0.0
 Identities = 1433/1433 (100%), Gaps = 0/1433 (0%)
 Strand=Plus/Plus

Query  14       AACCATATTGGAGGGCATCATGCCTGACGCTAAAAAACAGGGGCGGTCAAACAAGGCAAT  73
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3086921  AACCATATTGGAGGGCATCATGCCTGACGCTAAAAAACAGGGGCGGTCAAACAAGGCAAT  3086980

Query  74       GACGTTTTTCGTCTGCTTCCTTGCCGCTCTGGCGGGATTACTCTTTGGCCTGGATATCGG  133
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3086981  GACGTTTTTCGTCTGCTTCCTTGCCGCTCTGGCGGGATTACTCTTTGGCCTGGATATCGG  3087040

Query  134      TGTAATTGCTGGCGCACTGCCGTTTATTGCAGATGAATTCCAGATTACTTCGCACACGCA  193
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Sbjct  3087041   TGTAATTGCTGGCGCACTGCCGTTTATTGCAGATGAATTCCAGATTACTTCGCACACGCA  3087100

Query  194       AGAATGGGTCGTAAGCTCCATGATGTTCGGTGCGGCAGTCGGTGCGGTGGGCAGCGGCTG  253
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3087101   AGAATGGGTCGTAAGCTCCATGATGTTCGGTGCGGCAGTCGGTGCGGTGGGCAGCGGCTG  3087160

Query  254       GCTCTCCTTTAAACTCGGGCGCAAAAAGAGCCTGATGATCGGCGCAATTTTGTTTGTTGC  313
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3087161   GCTCTCCTTTAAACTCGGGCGCAAAAAGAGCCTGATGATCGGCGCAATTTTGTTTGTTGC  3087220

Query  314       CGGTTCGCTGTTCTCTGCGGCTGCGCCAAACGTTGAAGTACTGATTCTTTCCCGCGTTCT  373
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3087221   CGGTTCGCTGTTCTCTGCGGCTGCGCCAAACGTTGAAGTACTGATTCTTTCCCGCGTTCT  3087280

Query  374       ACTGGGGCTGGCGGTGGGTGTGGCCTCTTATACCGCACCGCTGTACCTCTCTGAAATTGC  433
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3087281   ACTGGGGCTGGCGGTGGGTGTGGCCTCTTATACCGCACCGCTGTACCTCTCTGAAATTGC  3087340

Query  434       GCCGGAAAAAAATTCGTGGCAGTATGATCTCGATGTATCAGTTGATGATCACTATCGGGAT  493
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3087341   GCCGGAAAAAAATTCGTGGCAGTATGATCTCGATGTATCAGTTGATGATCACTATCGGGAT  3087400

Query  494       CCTCGGTGCTTATCTTTCTGATACCGCCTTCAGCTACACCGGTGCATGGCGCTGGATGCT  553
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3087401   CCTCGGTGCTTATCTTTCTGATACCGCCTTCAGCTACACCGGTGCATGGCGCTGGATGCT  3087460

Query  554       GGGTGTGATTATCATCCCGGCAATTTTGCTGCTGATTGGTGTCTTCTTCCTGCCAGACAG  613
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3087461   GGGTGTGATTATCATCCCGGCAATTTTGCTGCTGATTGGTGTCTTCTTCCTGCCAGACAG  3087520

Query  614       CCCACGTTGGTTTGCCGCCAAACGCCGTTTTGTTGATGCCGAACGCGTGCTGCTACGCCT  673
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3087521   CCCACGTTGGTTTGCCGCCAAACGCCGTTTTGTTGATGCCGAACGCGTGCTGCTACGCCT  3087580

Query  674       GCGTGACACCAGCGCGGAAGCGAAACGCGAACTGGATGAAATCCGTGAAAGTTTGCAGGT  733
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3087581   GCGTGACACCAGCGCGGAAGCGAAACGCGAACTGGATGAAATCCGTGAAAGTTTGCAGGT  3087640

Query  734       TAAACAGAGTGGCTGGGCGCTGTTTAAAGAGAACAGCAACTTCCGCCGCGCGGTGTTCCT  793
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3087641   TAAACAGAGTGGCTGGGCGCTGTTTAAAGAGAACAGCAACTTCCGCCGCGCGGTGTTCCT  3087700

Query  794       TGGCGTACTGTTGCAGGTAATGCAGCAATTCACCGGGATGAACGTCATCATGTATTACGC  853
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3087701   TGGCGTACTGTTGCAGGTAATGCAGCAATTCACCGGGATGAACGTCATCATGTATTACGC  3087760

Query  854       GCCGAAAATCTTCGAACTGGCGGGTTATACCAACACTACCGAGCAAATGTGGGGGACCGT  913
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3087761   GCCGAAAATCTTCGAACTGGCGGGTTATACCAACACTACCGAGCAAATGTGGGGGACCGT  3087820

Query  914       GATTGTCGGCCTGACCAACGTACTTGCCACCTTTATCGCAATCGGCCTTGTTGACCGCTG  973
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3087821   GATTGTCGGCCTGACCAACGTACTTGCCACCTTTATCGCAATCGGCCTTGTTGACCGCTG  3087880

Query  974       GGGACGTAAACCAACGCTAACGCTGGGCTTCCTGGTGATGGCTGCTGGCATGGGCGTACT  1033
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3087881   GGGACGTAAACCAACGCTAACGCTGGGCTTCCTGGTGATGGCTGCTGGCATGGGCGTACT  3087940
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Query  1034     CGGTACAATGATGCATATCGGTATTCACTCTCCGTCGGCGCAGTATTTCGCCATCGCCAT  1093
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3087941  CGGTACAATGATGCATATCGGTATTCACTCTCCGTCGGCGCAGTATTTCGCCATCGCCAT  3088000

Query  1094     GCTGCTGATGTTTATTGTCGGTTTTGCCATGAGTGCCGGTCCGCTGATTTGGGTACTGTG  1153
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3088001  GCTGCTGATGTTTATTGTCGGTTTTGCCATGAGTGCCGGTCCGCTGATTTGGGTACTGTG  3088060

Query  1154     CTCCGAAATTCAGCCGCTGAAAGGCCGCGATTTTGGCATCACCTGCTCCACTGCCACCAA  1213
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3088061  CTCCGAAATTCAGCCGCTGAAAGGCCGCGATTTTGGCATCACCTGCTCCACTGCCACCAA  3088120

Query  1214     CTGGATTGCCAACATGATCGTTGGCGCAACGTTCCTGACCATGCTCAACACGCTGGGTAA  1273
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3088121  CTGGATTGCCAACATGATCGTTGGCGCAACGTTCCTGACCATGCTCAACACGCTGGGTAA  3088180

Query  1274     CGCCAACACCTTCTGGGTGTATGCGGCTCTGAACGTACTGTTTATCCTGCTGACATTGTG  1333
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3088181  CGCCAACACCTTCTGGGTGTATGCGGCTCTGAACGTACTGTTTATCCTGCTGACATTGTG  3088240

Query  1334     GCTGGTACCGGAAACCAAACACGTTTCGCTGGAACATATTGAACGTAATCTGATGAAAGG  1393
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3088241  GCTGGTACCGGAAACCAAACACGTTTCGCTGGAACATATTGAACGTAATCTGATGAAAGG  3088300

Query  1394     TCGTAAACTGCGCGAAATAGGCGCTCACGATTAATCTCCCCAAGCTTCCTCCC  1446
                ||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3088301  TCGTAAACTGCGCGAAATAGGCGCTCACGATTAATCTCCCCAAGCTTCCTCCC  3088353
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